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PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Beyaert et al.

Serial No.: 10/680,998

Filed: October 8, 2003

For: NOVEL INHIBITORS OF NF-kappaB  
ACTIVATION

Confirmation No.: 7433

Examiner: A. Rooke

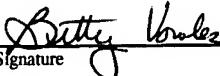
Group Art Unit: 1656

Attorney Docket No.: 2676-4554.1US

CERTIFICATE OF MAILING

I hereby certify that this correspondence along with any attachments referred to or identified as being attached or enclosed is being deposited with the United States Postal Service as First Class Mail on the date of deposit shown below with sufficient postage and in an envelope addressed to the Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

October 24, 2007  
Date

  
Signature

Betty Vowles  
Name (Type/Print)

COMMUNICATION

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

Included with this Communication is an executed Declaration. This Declaration corrects a typographical error in the Declaration submitted electronically on October 10, 2007.

Respectfully submitted,



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DJM/bv



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DECLARATION UNDER 37 C.F.R. § 1.132 OF DR. RUDI BEYAERT

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Dr. Rudi Beyaert hereby declares:

1. I am a named inventor on the above-referenced patent application.
2. I am a Professor at the University of Ghent and an expert in the field of molecular signal transduction. A copy of my curriculum vitae is attached.
3. I understand that in the Office Action mailed June 1, 2007, the Examiner has rejected claims 21 and 22 as assertedly lacking written description and enablement
4. Submitted herewith are a published research paper (Wullaert *et al.*, J. Biol. Chem. 282:1 81-90, Jan. 5, 1997) and some additional data showing that Poly (I:C) (additional data), LPS (additional data and Wullaert *et al.* at FIG. 4B), BCL10 (additional data), API2-MLT (additional data), MyD88 (Wullaert *et al.* at FIG. 6), IRAK1 (Wullaert *et al.* at FIG. 6), TLR4

(Wullaert *et al.* at FIG. 4A), and TRAF6 (Wullaert *et al.* at FIG. 6) are all equivalents of TNF, IL-1, TPA, RIP, and TRAF2 in terms of each being a means for inducing activation of the NF-kB pathway, wherein the means is inhibitable by an ABIN consensus sequence protein.

5. I understand that claim 21 currently recites:

A method of screening a compound for its ability to activate or suppress ABIN (A20-Binding Inhibitor of NF-kB activation) dependent NF-kB inhibition, said method comprising:

- a) combining a compound to be screened with a protein comprising ABIN amino acid consensus sequence of SEQ ID NO:9 and having the ability to inhibit NF-kB activation,
- b) detecting an interaction between said compound and said protein,
- c) identifying compounds that interact with said protein,
- d) obtaining a cell line with a nucleic acid sequence encoding said ABIN consensus sequence protein and an NF-kB dependent reporter gene,
- e) administering to the cell line a means for inducing activation of the NF-kB pathway, wherein the means is inhibitable by said ABIN consensus sequence protein,
- f) administering one of the detected compounds to said cell line, and
- g) determining if the administration of the detected compound alters NF-kB dependent reporter gene expression, wherein an increase in expression indicates that the detected compound suppresses ABIN dependent NF-kB inhibition and a decrease in expression indicates that the detected compound activates ABIN dependent NF-kB inhibition.

6. I understand that claim 22 currently recites:

The method according to claim 21, wherein obtaining a cell line comprises obtaining a cell line including a nucleic acid sequence encoding protein A20.

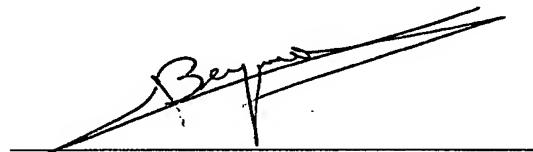
7. A person skilled in the art would know how to make and use the invention of claims 21 and 22 as TNF, IL-1, TPA, RIP, and TRAF2 are all described in the patent application in such a way as to indicate their ability to perform the function of "a means for inducing activation of the NF-kB pathway, wherein the means is inhibitable by an ABIN consensus sequence protein."

8. Such means are definite as one skilled in the art will understand what materials disclosed in the patent application (e.g. TNF, IL-1, TPA, RIP, and TRAF2) would perform the function of "a means for inducing activation of the NF-kB pathway, wherein the means is inhibitable by an ABIN consensus sequence protein."

9. A person skilled in the art would find adequate written description of a means for inducing activation of the NF-kB pathway, wherein the means is inhibitable by an ABIN consensus sequence protein as, e.g., TNF, IL-1, TPA, RIP, and TRAF2 are described in the patent application as being capable of performing that function.

10. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patents issued thereon.

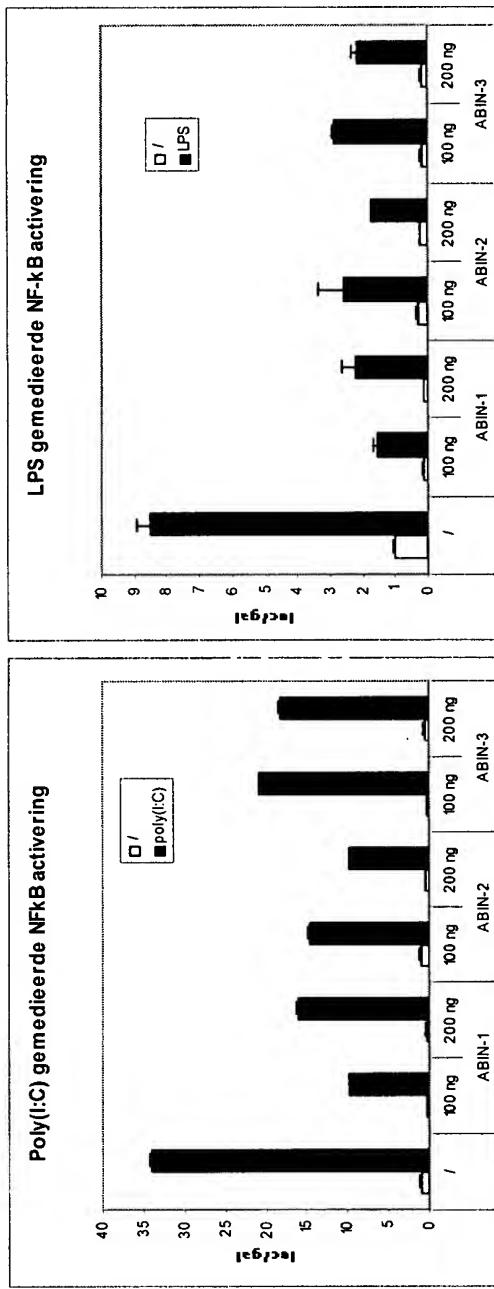
Date: October 2, 2007

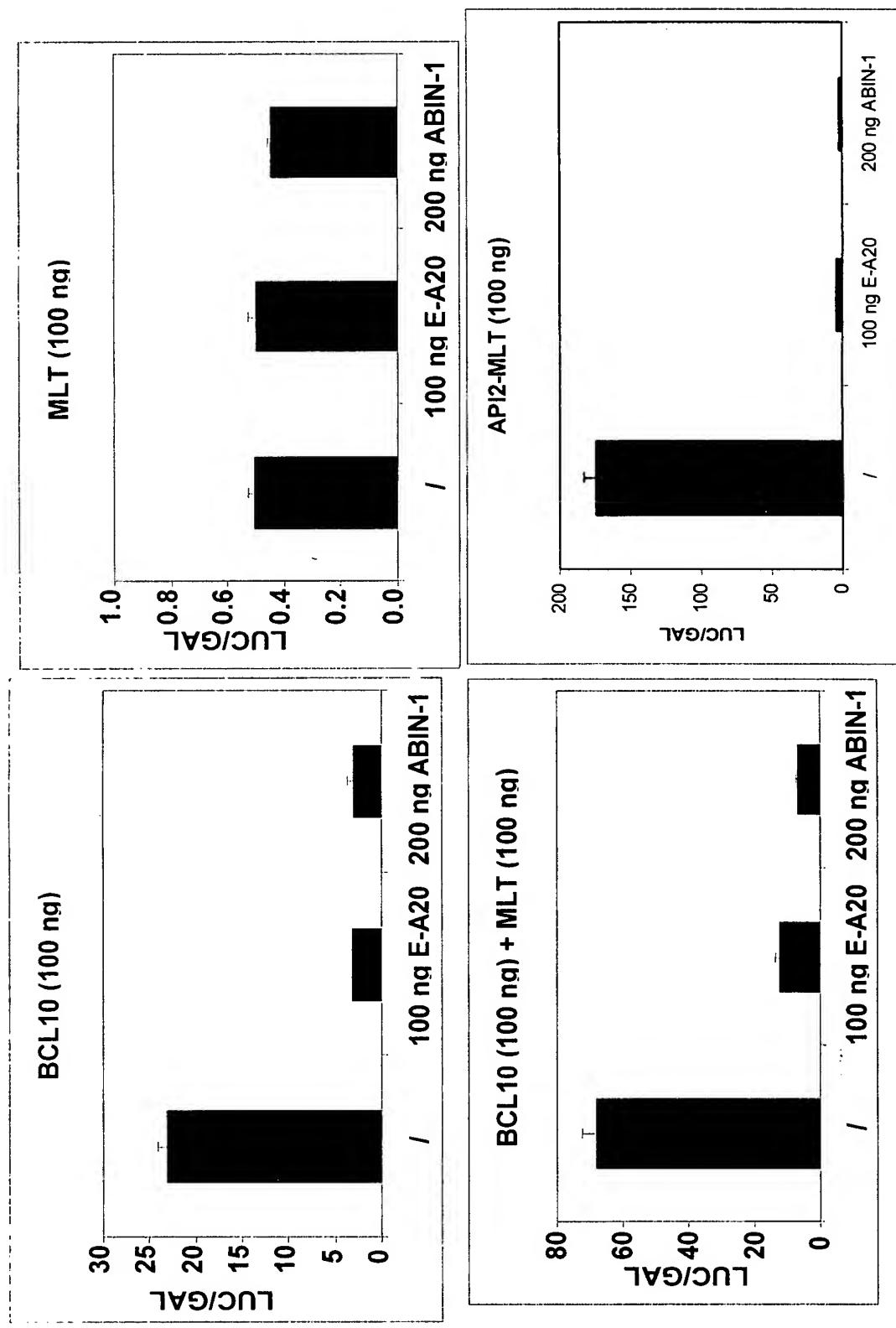


Dr. Rudi Beyaert

A handwritten signature of "Beyaert" is written over a diagonal line. Below the line, the name "Dr. Rudi Beyaert" is printed in a standard font.

# ABINs inhibit poly(I:C) and LPS induced NF- $\kappa$ B activation in respectively HEK-TLR3 and HEK-TLR4 cells





ABIN-1 inhibits Bcl10, Bcl10/MLT and API2/MLT induced NF- $\kappa$ B activation (= T cell and B cell receptor induced NF- $\kappa$ B activation)